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MyDate=Thu Aug 01 14:19:35 GMT-0400 (Eastern Daylight Time) 2002

submitto=Biotech01@uspto.gov

Name=Holly Schnizer

Empno=76558

Phone=703-3053722

Artunit=1653

Office=CM1 9E09

Serialnum=09/673,412

PatClass=424/450; 530/383

Earliest=4-27-98

Format1=paper

Format3=email

Searchtopic=The search topic is a pharmaceutical composition (for treating hemophilia) comprising factor VIII (FVIII) and a liposome.

The liposome is a "substantially neutral colloidal particle" and comprises 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer. The polymer has no net charge.

The FVIII is not encapsulated in the particle (liposome).

Examples of the lipid include: egg-phosphytidylcholine (PC) (lecithin),

Point of Contact:
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

Searcher: M. Smith
Phone: _____
Location: _____
Date Picked Up: 8/8/02
Date Completed: 8/29/02
Searcher Prep/Review: 65
Clerical: _____
Online time: 60

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: X
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____

DATE Rec'd in office
9-3-02

phosphatidylethanolamine (egg

Examples of the polymer include: polymers from the polyalkylether, polylactic and polyglycolic acid families and more specifically polyethylene glycol.

The liposome used in the examples is Egg phosphatidylcholine/polyethyleneglycol-phosphatidyl ethanloamine (E-PC/PEG-PE).

Thank you.

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Online time: _____

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____

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         (c) 2002 Inst for Sci Info
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         (c) 2002 Cambridge Sci Abs
File  94:JICST-EPlus 1985-2002/Jun W5
         (c)2002 Japan Science and Tech Corp(JST)
File 144:Pascal 1973-2002/Aug W4
         (c) 2002 INIST/CNRS
File 164:Allied & Complementary Medicine 1984-2002/Aug
          (c) 2002 BLHCIS
File 342:Derwent Patents Citation Indx 1978-01/200210
         (c) 2002 Thomson Derwent
File 345:Inpadoc/Fam.& Legal Stat 1968-2002/UD=200233
         (c) 2002 EPO
File 347:JAPIO Oct 1976-2002/Apr(Updated 020805)
         (c) 2002 JPO & JAPIO
File 351:Derwent WPI 1963-2002/UD,UM &UP=200255
         (c) 2002  Thomson Derwent
File 357:Derwent Biotech Res. 1982-2002/June W1
         (c) 2002 Thomson Derwent & ISI
File 358:Current BioTech Abs 1983-2001/Oct
          (c) 2001 DECHEMA
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2002/Aug 29
         (c) 2002 Inst for Sci Info
?ds

Set     Items   Description
S1        241   (FACTORVIII OR FACTOR(W)VIII OR FVIII) AND (LIPOSOME? OR L-
              IPID? OR EGG(W)PHOSPHYTIDYLCHOLINE? OR EPC OR LECITHIN? OR PE-
              G(W))PE) AND HEMOPHIL?
S2        142   RD (unique items)
S3         89   S2 AND (THERAP? OR PHARM? OR DRUG? OR MEDIC?)
S4          1   S3 AND (PHOSPHATIDYLETHANOLAMINE? OR PHOSPHATIDYL(W)ETHANO-
              LAMINE?)
?t4/7/1

 4/7/1     (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI
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014270998
WPI Acc No: 2002-091699/200213
  New cationic peptides capable of causing membrane disruption useful for
  preparing a complex for transferring an anionic substance of interest,
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e.g. a nucleic acid molecule into a cell for gene therapy applications
Patent Assignee: TRANSGENE SA (TRGE); JACOBS E (JACO-I); RITTNER K (RITT-I)
Inventor: JACOBS E; RITTNER K
Number of Countries: 029 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
EP 1161957	A1	20011212	EP 2001111145	A	20010509	200213 B
AU 200148015	A	20011129	AU 200148015	A	20010524	200213
CA 2346163	A1	20011126	CA 2346163	A	20010525	200213
US 20020055174	A1	20020509	US 2000246083	P	20001107	200235
			US 2001277982	P	20010323	
			US 2001865553	A	20010529	

Priority Applications (No Type Date): US 2001277982 P 20010323; EP 2000440162 A 20000526; US 2000246083 P 20001107; EP 2001440049 A 20010227
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 1161957	A1	E	67	A61K-047/48	
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
AU 200148015	A			C07K-007/08	
CA 2346163	A1	E		C07K-007/08	
US 20020055174	A1			C12N-015/87	Provisional application US 2000246083
					Provisional application US 2001277982

Abstract (Basic): EP 1161957 A1

NOVELTY - A cationic peptide (I) capable of causing membrane disruption and which does not comprise acidic amino acid, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a complex (II) capable of transferring an anionic substance of interest into a cell, comprising (I) and an anionic substance of interest; and

(2) use of (II) for the preparation of a pharmaceutical composition for curative, preventative or vaccine treatment of mammals;

(3) use of (I) for the preparation of (II) for transferring an anionic substance of interest into a cell.

ACTIVITY - Antidiabetic; cytostatic; hemostatic.

MECHANISM OF ACTION - Gene therapy ; vaccine. The potential of gene transfer with mono-component peptide vectors was investigated in vivo. 50 or 60 micrograms of the luciferase expression plasmid pTG11236 was complexed with pcTG90/dioleyl phosphatidylethanolamine (DOPE) (1:2) (+/-) 10 in 250 microliters 5 % glucose (Meyer et al.2000). The resulting lipoplex vector served as reference for gene transfer studies with pTG11236 complexed with ppTG1, ppTG20 and ppTG32 in 250 microliters 5 % glucose. 5 mice/group were intravenously injected, and the animals sacrificed at day 1 after injection. Lungs were tested for luciferase activity. The results demonstrated that gene transfer with ppTG1 complexes led to luciferase activities in the lung which were comparable to those obtained with the lipoplexes. Gene transfer with ppTG20 showed a general tendency to be more efficient and less toxic than ppTG1, while complexes with the peptide ppTG32 did not lead to detectable reporter gene expression. Complexes with ppTG1 were compared to those formed with control peptides JTS-1-K13, KALA, K8-NLSm/JTS-1 and ppTG20. KALA and K8-NLSm/JTS-1 were inefficient (data not shown). Luciferase activities observed in the lung at day 1 after intravenous injection of 50 microg pTG11236 complexed with ppTG1, JTS-1-K13 and ppTG20 indicated that gene transfer with ppTG1 was better than with JTS-1-K13. Gene transfer with ppTG20 showed the reproducible tendency

to give rise to higher gene expression and was less toxic than ppTG1. ppTG20 gave rise to more efficient gene transfer than ppTG1, while ppTG20-D (ppTG20 derivative with all amino acids in D-configuration) was more efficient than ppTG20.

Gly Leu Phe Lys Ala Leu Leu Lys Leu Leu Lys Ser Leu Trp Lys Leu Leu Leu Lys Ala (ppTG1)

Gly Leu Phe Arg Ala Leu Leu Arg Leu Leu Arg Ser Leu Trp Arg Leu Leu Leu Arg Ala (ppTG20)

Gly Val Phe Lys Ala Val Val Lys Val Val Lys Ser Val Trp Lys Val Val Val Lys Ala (ppTG32)

USE - (I) is useful for preparing a complex (II) for transferring an anionic substance of interest into a cell, particularly a nucleic acid comprising a therapeutically useful gene sequence and elements enabling its expression. (II) is useful in the preparation of a pharmaceutical composition for curative, preventive or vaccine treatment of mammals (claimed). (I) modified with a detectable group is useful for diagnostic purposes (e.g. imaging of tumoral cells and transformed cells). (II) is useful for delivering anionic substance into a cell, particularly in gene therapy applications. (II) comprises the gene encoding factor VIII or IX for treating hemophilia A or B, dystrophin in the context of myopathies, insulin in the context of diabetes, cystic fibrosis transmembrane conductance regulator in the context of cystic fibrosis or suitable anti-tumor genes. (I) is capable of interacting with a membrane, particularly with a cellular membrane, and more particularly with an endosomal and/or lysosomal membrane, such that the interaction results in destabilizing and/or leaking of the membrane, and particularly in freeing the contents of the endosomes.

pp; 67 DwgNo 0/11

Derwent Class: B04; D16
International Patent Class (Main): A61K-047/48; C07K-007/08; C12N-015/87
International Patent Class (Additional): A61K-039/00; A61K-047/42; A61K-047/44; A61K-048/00; C07K-014/00; C07K-014/47; C07K-016/44; C12N-015/88

?ds

Set	Items	Description
S1	241	(FACTORVIII OR FACTOR(W)VIII OR FVIII) AND (LIPOSOME? OR L-IPID? OR EGG(W)PHOSPHYTIDYLCHOLINE? OR EPC OR LECITHIN? OR PE-G(W))PE) AND HEMOPHIL?
S2	142	RD (unique items)
S3	89	S2 AND (THERAP? OR PHARM? OR DRUG? OR MEDIC?)
S4	1	S3 AND (PHOSPHATIDYLETHANOLAMINE? OR PHOSPHATIDYL(W)ETHANO-LAMINE?)
S5	1	S3 AND BIOCOMPATIBLE(W)HYDROPHILIC(W)POLYMER?
S6	1	S5 NOT S4

?t6/7/1

6/7/1 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

012880943
WPI Acc No: 2000-052777/200004
Parenteral composition containing active protein attached to, but not encapsulated in, colloid particles containing a lipid modified with polymer, particularly for treating hemophilia
Patent Assignee: OPPERBAS HOLDING BV (OPPE-N)
Inventor: BAR L; BARU M; NUR I
Number of Countries: 087 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9955306	A1	19991104	WO 99IL217	A	19990423	200004 B
AU 9934414	A	19991116	AU 9934414	A	19990423	200015
BR 9909978	A	20001226	BR 999978	A	19990423	200103
			WO 99IL217	A	19990423	
EP 1079805	A1	20010307	EP 99916022	A	19990423	200114
			WO 99IL217	A	19990423	
JP 2002512947	W	20020508	WO 99IL217	A	19990423	200234
			JP 2000545506	A	19990423	
AU 747391	B	20020516	AU 9934414	A	19990423	200244

Priority Applications (No Type Date): IL 124224 A 19980427
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9955306	A1	E	30	A61K-009/127	
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
AU 9934414	A				Based on patent WO 9955306
BR 9909978	A			A61K-009/127	Based on patent WO 9955306
EP 1079805	A1	E		A61K-009/127	Based on patent WO 9955306
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002512947	W		28	A61K-038/43	Based on patent WO 9955306
AU 747391	B			A61K-009/127	Previous Publ. patent AU 9934414
					Based on patent WO 9955306

Abstract (Basic): WO 9955306 A1

NOVELTY - Parenteral composition (A) comprises:

(i) therapeutic amount of a protein or polypeptide (I); and

(ii) neutral colloidal particles (CP) that comprise 1-20 mole% of an amphipathic lipid (II) derivatized with a biocompatible hydrophilic polymer (III) that has no net charge.

(I) either binds to CP or can bind poly(ethylene glycol) (PEG), but is not encapsulated in CP

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for treatment of hemophilia by administration of (A) in which (I) is coagulation factor VIII (F8).

ACTIVITY - Anti- hemophilia .

MECHANISM OF ACTION - None given.

USE - Where (I) is F8 (no other suitable (I) are indicated), the compositions are used to treat hemophilia , particularly in patients who have developed F8-inhibitory (neutralizing) antibodies.

ADVANTAGE - In these formulations, (I) binds to the derivatized (II) so its half-life is increased (it is expected to be effective for 24 hours); it is protected against neutralizing antibodies present in serum and is released slowly. Since CP does not encapsulate (I), smaller particles can be used which are not retained in the reticulo-endothelial system so persist for longer. (III) stabilizes the particles against fusion and because interaction between (III) and (I) is not covalent, chemical activation of (III) is not necessary.

pp; 30 DwgNo 0/1

Derwent Class: A96; B04
International Patent Class (Main): A61K-009/127; A61K-038/43
International Patent Class (Additional): A61K-009/50; A61K-038/37; A61K-047/24; A61K-047/34; A61P-007/04
?t8/7/1-4

8/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06018637 89111305 PMID: 3145997
Improvement in anti- hemophilic preparations and its problems. 5. Stability and oral administration of factor VIII and IX concentrates]
Oguma Y; Shimizu K; Sakuragawa N
Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) May 1988, 29 (5) p655-61, ISSN 0485-1439 Journal Code: 2984782R
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
Record Date Created: 19890302

8/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04996604 86071422 PMID: 3934801
Inactivation of viruses in labile blood derivatives. I. Disruption of lipid -enveloped viruses by tri(n-butyl)phosphate detergent combinations.
Horowitz B; Wiebe M E; Lippin A; Stryker M H
Transfusion (UNITED STATES) Nov-Dec 1985, 25 (6) p516-22, ISSN 0041-1132 Journal Code: 0417360
Contract/Grant No.: NO1-HB-3-7009; HB; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Use of the organic solvent, tri(n-butyl)phosphate (TNBP), and detergents for the inactivation of viruses in labile blood derivatives was evaluated by addition of marker viruses (VSV, Sindbis, Sendai, EMC) to anti-hemophilic factor (AHF) concentrates. The rate of virus inactivation obtained with TNBP plus Tween 80 was superior to that observed with ethyl ether plus Tween 80, a condition previously shown to inactivate greater than or equal to 10(6.9) CID50 of hepatitis B and greater than or equal to 10(4) CID50 of Hutchinson strain non-A, non-B hepatitis. The AHF recovery after TNBP/Tween treatment was greater than or equal to 90 percent. Following the reaction, TNBP could be removed from the protein by gel exclusion chromatography on Sephadex G25; however, because of its large micelle size, Tween 80 could not be removed from protein by this method. Attempts to remove Tween 80 by differential precipitation of protein were only partially successful. An alternate detergent, sodium cholate, when combined with TNBP, resulted in almost as efficient virus inactivation and an 80 percent recovery of AHF. Because sodium cholate forms small micelles, it could be removed by Sephadex G25 chromatography. Electrophoretic examination of TNBP/cholate-treated AHF concentrates revealed few, if any, changes in protein mobility, except for plasma lipoprotein(s).
Record Date Created: 19851224

8/7/3 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

014436505 **Image available**
WPI Acc No: 2002-257208/200230
Managing anticoagulation therapy in a patient involves administering

acute phase anticoagulant during acute phase of coagulation and active-site inhibited factor VIIa polypeptide during chronic phase of coagulation
Patent Assignee: UNIV MINNESOTA (MINU)
Inventor: NELSESTUEN G L
Number of Countries: 096 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200203075	A2	20020110	WO 2001US20307	A	20010626	200230 B
AU 200170171	A	20020114	AU 200170171	A	20010626	200237

Priority Applications (No Type Date): US 2000607716 A 20000630
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200203075	A2	E	90	G01N-033/86	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200170171	A		G01N-033/86	Based on patent WO 200203075

Abstract (Basic): WO 200203075 A2
NOVELTY - Managing (I) anticoagulation therapy in a patient comprises administering an acute phase anticoagulant to the patient during the acute phase of coagulation, and administering a chronic phase anticoagulant to the patient during the chronic phase of coagulation.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) evaluating (II) patient responsiveness to factor VIIa or activated protein C (APC) therapy by adding factor VIIa or APC to whole blood sample and monitoring activated clotting time (ACT) of blood sample in absence of added phospholipid , where significant decrease in ACT compared to control sample from patient in the absence of added factor VIIa or APC indicates that patient is responsive to factor VIIa or APC;
(2) detecting (III) tissue factor in blood, by obtaining an anticoagulated blood sample, neutralizing factor VIII or IX and neutralizing tissue factor in the anticoagulated blood sample and assaying ACT of the anticoagulated blood sample in the presence of added factor VIIa, where the presence or absence of tissue factor is detected by comparing ACT of the anticoagulated blood sample relative to a corresponding anticoagulated blood sample without neutralized tissue factor;
(3) evaluating (IV) dosage of APC, by obtaining a whole blood sample from a patient undergoing APC therapy , and monitoring ACT of the whole blood sample in the absence of added phospholipid , where a significant increase in ACT compared to a control sample from the patient before APC therapy indicates that an appropriate dosage of APC has been administered;
(4) a kit (V) for detecting tissue factor, comprising anti- factor VIII or anti-factor IX antibody, an anticoagulant and factor VIIa; and
(5) a kit (VI) for detecting factor VIIa or APC in blood, comprising a Ca2+ chelator, a calcium salt and an activator of contact phase of coagulation.
ACTIVITY - Thrombolytic; Anticoagulant.
No supporting data is given.
MECHANISM OF ACTION - Regulator of coagulation.

USE - (I) is useful for managing anticoagulation therapy . (II) is useful for monitoring patient responsiveness to factor VIIa or APC. The assays provides the ability to detect genetic disorders such as APC resistance or protein S deficiency. (III) is useful to screen or diagnose coagulation disorders that result in altered tissue factor expression in the circulation e.g. arteriosclerosis or cancer. (IV) is useful for evaluating the dosage of APC.

ADVANTAGE - Modifications to vitamin K-dependent polypeptides increase their circulation half-life and their activity, and also reduce the amount of protein needed to treat clotting disorders as well as decrease the frequency of the administration. The method allows individual patients to be monitored such that therapies can be tailored, minimizing costs associated with such therapies . The methods have excellent reproducibility.

pp; 90 DwgNo 2A/16

Derwent Class: A96; B04; S03

International Patent Class (Main): G01N-033/86

8/7/4 (Item 2 from file: 351)

DIALOG(R)File 351:Derwent WPI

013905738

WPI Acc No: 2001-389951/200141

Bioreactor for systemic delivery of bioactive agents, comprises nucleic acids encoding growth stimulating and bioactive agents, and a biocompatible substance capable of cellular infiltration

Patent Assignee: SELECTIVE GENETICS INC (SELE-N); CHANDLER L A (CHAN-I); PIERCE G (PIER-I)

Inventor: CHANDLER L A; PIERCE G

Number of Countries: 094 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200140272	A2	20010607	WO 2000US32754	A	20001130	200141	B
AU 200119398	A	20010612	AU 200119398	A	20001130	200154	
US 20010044413	A1	20011122	US 99168470	A	19991201	200176	
			US 2000729644	A	20001130		

Priority Applications (No Type Date): US 99168470 P 19991201; US 2000729644 A 20001130

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200140272	A2	E	69	C07K-014/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200119398	A	C07K-014/00	Based on patent WO 200140272
US 20010044413	A1	A61K-048/00	Provisional application US 99168470

Abstract (Basic): WO 200140272 A2

NOVELTY - An in situ bioreactor (I) adapted for systemic delivery of bioactive agents, comprising a nucleic acid encoding a growth stimulating agent, a nucleic acid encoding a bioactive agent, and a biocompatible substance capable of cellular infiltration, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) systemic delivery of a protein from a tissue site in an animal,

comprising contacting the tissue site with (I);

(2) a Bi-gene device comprising a biocompatible substance capable of cellular infiltration, a nucleic acid encoding a cell growth stimulating agent, and a second nucleic acid encoding a bioactive agent;

(3) a kit for the production of a device comprising:

(a) a container;

(b) a biocompatible substance;

(c) a nucleic acid encoding a cell growth stimulating agent; and

(d) a second nucleic acid encoding a bioactive agent; and

(4) a kit for the production of a coated device comprising:

(a) a device coated with a biocompatible substance;

(b) a nucleic acid encoding a growth stimulating agent; and

(c) a second nucleic acid encoding a bioactive agent.

ACTIVITY - Vulnerary; hemostatic; antianemic; antidiabetic; antiarthritic; coagulant; antiinflammatory; immunosuppressive; neuroprotective; cytostatic; antirheumatic; osteopathic; anti-infertility; contraception.

MECHANISM OF ACTION - Bioactive agent deliverer; protein and gene therapy .

USE - (I) is used for cellular ingrowth and systemic delivery of a bioactive agent, such as a protein from a tissue site in an animal (claimed). (I) is used as an implant. (I) can be used to treat conditions associated with renal dialysis, hemophilia , hemoglobinopathies, thalassemias, anemia, lipid storage disease, mucopolysaccharidoses, diabetes, hypercoagulability, arthritis, hypercoagulability, stroke, cerebroprotective, inflammation, infection, autoimmunity, multiple sclerosis, thrombocytopenia, cancer, osteoporosis, infertility, and birth control.

ADVANTAGE - (I) allows sustained and controlled gene delivery as well as sustained product expression using in vivo transfer and expression of desired nucleic acids.

pp; 69 DwgNo 0/3

Derwent Class: A14; A17; A28; A89; B04; B07; D16; D22

International Patent Class (Main): A61K-048/00; C07K-014/00

?

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FILE LAST UPDATED: 27 Aug 2002  (20020827/ED)

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=> d stat que
L1             3 SEA FILE=REGISTRY "FACTOR VIII"/CN
L5            33 SEA FILE=REGISTRY PHOSPHATIDYLETHANOLAMINE?/CN
L6             1 SEA FILE=REGISTRY PEG-PE/CN
L12         8946 SEA FILE=HCAPLUS L1 OR FACTOR(W)VIII OR FACTORVIII OR FVIII
L13         1275 SEA FILE=HCAPLUS EGG(W)PHOSPHYTIDYLCHOLINE? OR EPC OR EGGPHOSPH
               YTIDYLCHLINE?
L15        23308 SEA FILE=HCAPLUS L5 OR PHOSPHATIDYLETHANOLAMINE?
L16           97 SEA FILE=HCAPLUS L6 OR PEG(W)PE
L21           46 SEA FILE=HCAPLUS L12 AND (L13 OR L15 OR L16)
L22            5 SEA FILE=HCAPLUS L21 AND HEMOPHIL?


=> d ibib abs hitrn l22 1-5

L22  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1998:685052  HCAPLUS
DOCUMENT NUMBER:          129:272683
TITLE:                    Reagent for determining activated partial
                          thromboplastin time (aPTT)
INVENTOR(S):              Moritz, Berta; Varadi, Katalin; Lang, Hartmut;
                          Schwarz, Hans-Peter
PATENT ASSIGNEE(S):       Immuno A.-G., Austria
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
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LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844352	A1	19981008	WO 1998-AT82	19980326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AT 9700533	A	19990215	AT 1997-533	19970327
AT 405692	B	19991025		
AU 9863854	A1	19981022	AU 1998-63854	19980326
EP 972203	A1	20000119	EP 1998-909216	19980326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				

PRIORITY APPLN. INFO.: AT 1997-533 19970327
WO 1998-AT82 19980326

AB The invention concerns a lyophilized reagent and a test kit for the detn. of activated partial thromboplastin time (aPTT), consisting of coagulation factor(s), phospholipids, and an activator for intrinsic coagulation. Purified blood coagulation factors used are: Factor II, V, VII, VIII, IX, X, XI, XII, protein C, S, Z, their activated form, and combination. Activators are ellagic acids, celite, silicon contg. compds. and sulfatides, their derivs. and their combination. A mixt. of purified phospholipids is applied. The reagent is calcium ion free; it contains stabilizing agent(s), e.g. albumin, buffer substances, amino acid, sugar, gelatine or their combination. Further components are: a chromogenic agent, and anticoagulants. For performing the aPTT measurement the reagent is reconstituted in the presence of Ca ions. The measurement is applied for the detn. of activated protein C (APC) resistance, APC-cofactor activity, APC substrate, **factor VIII** deficiency and other protein C pathway related deficiencies. The test kit contains the lyophilized reagents and calibration material.

IT **113189-02-9**, Blood-coagulation **factor VIII**, procoagulant
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(reagent for detg. activated partial thromboplastin time (aPTT))

L22 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:516717 HCAPLUS
DOCUMENT NUMBER: 101:116717
TITLE: Antihemophilic compositions
INVENTOR(S): Barrowcliffe, Trevor William; Gray, Elaine; Kemball-Cook, Geoffrey
PATENT ASSIGNEE(S): National Biological Standards Board, UK
SOURCE: Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2129685	A1	19840523	GB 1983-29700	19831107
GB 2129685	B2	19851113		

PRIORITY APPLN. INFO.: GB 1982-32256 19821111

AB An antihemophilic compn. for i.v. administration comprises a mixt. of 2.5 .mu.g phospholipid/IU **Factor VIII** [**9001-27-8**]. The phospholipid contains .gtoreq.15% phosphatidylserine. A **factor VIII** prepn. (1 mL, 1.0 IU/mL) was incubated at 37.degree. for 20 min with a phospholipid (from human brain) emulsion (1 mL, 0.2 mg/mL). The incubate was then freeze-dried and stored in a sealed ampul under a N atm. at -20.degree..

IT **9001-27-8**
RL: BIOL (Biological study)
(antihemophilic compn. contg. phospholipids and)

L22 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:488685 HCAPLUS
DOCUMENT NUMBER: 101:88685
TITLE: Effect of phospholipid on **factor VIII** inactivation
AUTHOR(S): Barrowcliffe, T. W.; Kemball-Cook, G.; Gray, Elaine
CORPORATE SOURCE: Natl. Inst. Biol. Stand. Control, London, NW3 6RB, UK
SOURCE: Prog. Clin. Biol. Res. (1984), 150(Factor VIII Inhib.), 251-63
CODEN: PCBRD2; ISSN: 0361-7742
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies were made on the ability of 3 injectable, com. phospholipid (PL) prepns. to protect human blood coagulation **factor VIII** clotting activity (VIII:C) against antibody attack. One PL prepn. was inactive; the other 2 were only partially active and required much higher PL concns. than the std. PL from the National Institute for Biol. Stds. and Control in London, England. Studies with purified PLs demonstrated that the amt. of phosphatidylserine (PS) was crit.; a PS content of .gtoreq.20% was necessary for optimum VIII:C protection. PLs extd. from brain tissue appeared to be suitable in terms of PS content and biol. activity for VIII:C protection. Fractionation of the human antibodies used in the assays demonstrated the presence of 2 types of antibody, 1 directed against the PL binding site on antigen-bound VIII:C, and the other directed against other sites on the mol.

IT **9001-27-8**
RL: BIOL (Biological study)
(inactivation of, by antibodies, phospholipid prepns. effect on, of human)

L22 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:470380 HCAPLUS
DOCUMENT NUMBER: 101:70380

TITLE: The interaction between **factor VIII** clotting antigen and phospholipids in genetic variants of **hemophilia** and von Willebrand's disease
AUTHOR(S): Kobayashi, Isao; Lamme, Stefan; Nilsson, Inga Marie
CORPORATE SOURCE: Dep. Coagulation Disord., Univ. Lund, Malmoe, Swed.
SOURCE: Thromb. Res. (1984), 35(1), 65-75
CODEN: THBRAA; ISSN: 0049-3848
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of **factor VIII** with phospholipids was investigated in 11 patients with mild and moderate **hemophilia** A, 7 patients with von Willebrand's disease and in 10 healthy people as controls. The addn. of phospholipid vesicles contg. phosphatidylserine and **phosphatidylethanolamine** to normal plasma and that of patients with von Willebrand's disease resulted in the loss of almost two-thirds of the **factor VIII** clotting antigen (VIII:CAg). Defective interaction of phospholipids with VIII:CAg was noted in some genetic variants of mild and moderate **hemophilia** A. Thus, 4 of the 5 families tested showed decreased binding of VIII:CAg to phospholipids. One of the families tested belonged to a genetic variant with much more VIII:CAg than VIII:C, and it was in members of this family that the binding capacity was most reduced. The most probable explanations for the defective interaction with phospholipids is that mol. defects of VIII:CAg result in either decreased binding to phospholipids or might lead to a stronger binding between VIII:CAg and the von Willebrand factor in the **factor VIII** complex and thereby preventing the normal sepn. of the complex.

IT **9001-27-8**
RL: BIOL (Biological study)
(clotting antigen of, phospholipid interaction with, in genetic variants of **hemophilia** and von Willebrand's disease in human)

L22 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:158711 HCAPLUS
DOCUMENT NUMBER: 96:158711
TITLE: Erythrophosphatide-a reagent for coagulation studies
AUTHOR(S): Rakityanskaya, A. A.; Khomich, E. N.; Gilevskii, E. N.
CORPORATE SOURCE: Beloruss. Nauchno-Issled. Inst. Pereliv. Krovi, Minsk, USSR
SOURCE: Lab. Delo (1982), (1), 32-4
CODEN: LABDAZ; ISSN: 0023-6748
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The title erythrophosphatide (EP) reagent, prepd. from human erythrocytes, is useful in the study of blood coagulation. The EP reagent contains phosphatidylcholines .apprx.30, **phosphatidylethanolamines** 25, sphingomyelins 21, phosphatidylinositols 14, and phosphatidylserines 10%. The reagent at optimum concn. reduces blood coagulation time by 34% and in siliconized probes by 50.5%. It can be used in the thromboplastin formation test and in place of thrombocytes and cephalins. EP reagent can also be used to det. blood coagulation factors VIII and IX. A 3% emulsion of the reagent can be stored for 2 yr.

IT **9001-27-8**
RL: ANT (Analyte); ANST (Analytical study)

(detn. of, in humans, erythrophosphatide reagent for)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d stat que

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L1            3 SEA FILE=REGISTRY "FACTOR VIII"/CN
L4          637 SEA FILE=REGISTRY (LECITHIN/BI OR "LECITHIN:CHOLESTEROL"/BI OR
                LECITHINASE/BI OR LECITHINE/BI OR LECITHINOCLASTICUM/BI OR
                LECITHINOL/BI OR LECITHINOLYTICUM/BI OR LECITHINON/BI OR
                LECITHINS/BI)
L5           33 SEA FILE=REGISTRY PHOSPHATIDYLETHANOLAMINE?/CN
L6            1 SEA FILE=REGISTRY PEG-PE/CN
L7         1237 SEA FILE=REGISTRY LIPID/BI
L8           36 SEA FILE=REGISTRY LIPIDS/BI
L12        8946 SEA FILE=HCAPLUS L1 OR FACTOR(W)VIII OR FACTORVIII OR FVIII
L13        1275 SEA FILE=HCAPLUS EGG(W)PHOSPHYTIDYLCHOLINE? OR EPC OR EGGPHOSPH
                YTIDYLCHLINE?
L14       70324 SEA FILE=HCAPLUS L4 OR LECITHIN?
L15       23308 SEA FILE=HCAPLUS L5 OR PHOSPHATIDYLETHANOLAMINE?
L16          97 SEA FILE=HCAPLUS L6 OR PEG(W)PE
L17      329128 SEA FILE=HCAPLUS L7 OR L8 OR LIPID? OR ?LIPOSOME?
L21          46 SEA FILE=HCAPLUS L12 AND (L13 OR L15 OR L16)
L22           5 SEA FILE=HCAPLUS L21 AND HEMOPHIL?
L23      459285 SEA FILE=HCAPLUS THU/RL
L24     1133052 SEA FILE=HCAPLUS THERAP? OR PHARM? OR DRUG? OR MEDIC?
L25      400486 SEA FILE=HCAPLUS 62/SC OR 63/SC OR 64/SC
L26        1702 SEA FILE=HCAPLUS (L23 OR L24 OR L25) AND ?HEMOPHIL?
L27         832 SEA FILE=HCAPLUS L12 AND L26
L28          39 SEA FILE=HCAPLUS L27 AND (L14 OR L15 OR L16 OR L17)
L29          37 SEA FILE=HCAPLUS L28 NOT L22
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=> d ibib abs hitrn l29 1-37

L29 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:571737 HCAPLUS

TITLE: Spontaneous clots in normal plasma and in patients with **hemophilia** A

AUTHOR(S): Korotina, N. G.; Ovanesov, M. V.; Plyushch, O. P.; Kopylov, K. G.; Lopatina, E. G.; Saenko, E. L.; Butylin, A. A.; Ataullakhanov, F. I.

CORPORATE SOURCE: Gematol. Nauchnyi Tsentr, RAMN, Moscow, Russia

SOURCE: Gematologiya i Transfuziologiya (2002), 47(3), 26-30
CODEN: GETRE8; ISSN: 0234-5730

PUBLISHER: Izdatel'stvo Meditsina

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB In donor plasma in vitro after recalcification, even in the absence of the activators, clotting begins spontaneously in 10-20 min in a few centers. Later, spontaneous clots grow in size, filling up all plasma vol. The no. of the spontaneous centers diminished with lowering no. of plasma platelets. Ultracentrifugation of plasma (50000 g, 1 h, 21.degree.C) stops formation of the spontaneous centers. Return of 10% platelets or

microvesicules, produced of platelets in activation of A-23187, reestablishes spontaneous thrombogenic activity of plasma. The addn. of 0,1% erythrocytes or artificial phospholipid vesicles consisting of phosphatidylserine:phosphatidylcholine (25:75%) in concn. 10 mcM (on conversion to **lipids**) restores normal spontaneous activity. The inhibitor of the contact phase significantly decreases the no. of spontaneous centers. In plasma of **hemophiliacs** spontaneous clots do not form. In compensation of **factor VIII** (pVIII) deficiency in plasma of patients with severe **hemophilia** A, the no. of spontaneous clots increases. Normalization of spontaneous thrombogenesis occurs in 5% level of **factor VIII** compared to normal. Higher concns. of the factor lead to formation of spontaneous clots in quantities higher than in normal plasma. This points to hypercoagulatory properties of **hemophilic** plasma. The control over spontaneous clots may be used for monitoring of replacement **therapy** of **hemophilia** patients.

L29 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:546721 HCAPLUS
TITLE: Assaying the circulating **factor VIII** activity in **hemophilia** A patients treated with recombinant **factor VIII** products
AUTHOR(S): Mikaelsson, Marianne; Oswaldsson, Ulla
CORPORATE SOURCE: Biovitrum AB, Stockholm, SE-11276, Swed.
SOURCE: Seminars in Thrombosis and Hemostasis (2002), 28(3), 257-264
CODEN: STHMBV; ISSN: 0094-6176
PUBLISHER: Thieme Medical Publishers, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Large discrepancies between **factor VIII** assay methods have been reported from **pharmacokinetic** studies of recombinant **factor VIII** concs. In the assay of postinfusion patient plasma samples, traditional activated partial thromboplastin time (aPTT)-based one-stage clotting methods usually give results that are 20 to 50% lower than those obtained by chromogenic substrate assays. Investigations into the cause of these discrepancies have shown that the choice of phospholipid in the one-stage assay is crucial. The use of platelets or **liposomes** resembling platelet factor 3 instead of traditional aPTT reagents results in an increase in the apparent one-stage activity and a fairly good correlation with the chromogenic results. These and other functional test results, antigen measurements as well as clin. data, support the view that the chromogenic assay most accurately reflects the **therapeutic** effect. In addn. to the differences among assay methods, there is also a discrepancy between the World Health Organization (WHO) stds. for concs. and plasma. The use of product-specific stds., prepd. by dilg. the **factor VIII** conc. into **hemophilic** plasma, when assaying postinfusion plasma samples seems to be a feasible approach to overcome the problems encountered in **pharmacokinetic** studies.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:450690 HCAPLUS
DOCUMENT NUMBER: 137:57301
TITLE: Safety of **factor VIII** inhibitor bypass activity (FEIBA): 10-year compilation of thrombotic adverse events
AUTHOR(S): Ehrlich, H. J.; Henzl, M. J.; Gomperts, E. D.
CORPORATE SOURCE: Baxter BioScience, Vienna, A-1221, Austria
SOURCE: Haemophilia (2002), 8(2), 83-90
CODEN: HAEMF4; ISSN: 1351-8216
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Published and unpublished spontaneously reported thrombotic adverse events (AEs) in **factor VIII** inhibitor bypass activity (FEIBA) recipients were compiled for the most recent 10-yr period during which FEIBA units equiv. to 3.95.times.105 typical infusions were distributed worldwide. A total of 16 thrombotic AEs were documented over the 10-yr period, corresponding to an incidence of 4.05 per 105 infusions (95% CI, 2.32-6.58 per 105 infusions). Disseminated intravascular coagulation (n = 7) and myocardial infarction (n = 5) were the most frequent thrombotic AEs. One fatality occurred in an 87-yr-old metastatic cancer patients. In 13/16 (81%) patients known risk factors were present, most commonly FEIBA overdose in 8/16 (50%), obesity in 3/16 (19%) and serum **lipid** abnormalities in 2/16 (12%). These findings indicate that thrombotic AEs in FEIBA recipients are very rare. Recognition of risk factors and avoidance of FEIBA overdosage may avert thrombotic AEs.
IT **9001-27-8**, Blood coagulation **factor VIII**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; safety of **factor VIII** inhibitor bypass activity (FEIBA) based on 10-yr compilation of thrombotic adverse events)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:428652 HCAPLUS
DOCUMENT NUMBER: 137:10979
TITLE: Preparation of **antihemophilic** factor A-associated dispersion system
INVENTOR(S): Balasubramanian, Sathyamangalam V.; Besman, Marc; Kashi, Ramesh; Ramani, Karthik
PATENT ASSIGNEE(S): The Research Foundation of State University of New York, USA; Baxter Healthcare Corporation
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043665	A2	20020606	WO 2001-US48201	20011130

WO 2002043665 A3 20020711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-250137P P 20001130

AB A method for complexing AHF (**antihemophilic** factor A) in a dispersed medium, includes: providing an AHF protein, altering the conformational state of the AHF protein to expose hydrophobic domains therein, binding a stabilizer to the exposed hydrophobic domains, and at least partially reversing the alteration to assoc. at least a portion of the protein with the stabilizer. A stabilized AHF dosage form, wherein >25% of the AHF mol., is assocd. with a stabilizer is also disclosed. DMPC, brain phosphatidylserines, and cholesterol were dissolved in chloroform and the solvent was removed. The multilamellar vesicles thus formed were filtered through a polycarbonate filter to form small unilamellar (SUVs) below 200 nm. The **liposomes** encapsulating the protein were formed by mixing the **liposomes** in protein (AHF) contg. buffer and ethanol followed by gentle swirling .gtoreq.37.degree. to generate intermediate structures. The PEGyation of these particles were performed by adding DSPE-PEG.

IT **113189-02-9**, Blood coagulation **factor VIII**
RL: PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of **antihemophilic** factor A-assocd. dispersion system)

IT **18656-38-7**, DMPC
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of **antihemophilic** factor A-assocd. dispersion system)

L29 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:402663 HCAPLUS
TITLE: Preliminary experimental research on gene **therapy** for **hemophilia** A
AUTHOR(S): Yin, Jun; Wang, Hongli; Hu, Yiqun; Wang, Xuefeng; Qu, Bin; Chu, Haiyan; Duan, Baohua; Kang, Wenying; Qi, Zhengwu; Wang, Zhenyi
CORPORATE SOURCE: Shanghai Institute of Hematology, Ruijin Hospital, Shanghai Second Medical University, Shanghai, 200025, Peop. Rep. China
SOURCE: Zhonghua Xueyexue Zazhi (2002), 23(3), 138-142
CODEN: CHTCD7; ISSN: 0253-2727
PUBLISHER: Zhongguo Yixue Kexueyuan Xueyexue Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A kind of **therapeutic** gene for **hemophilia** A was developed, which could express human **factor VIII**(hF VIII) in vivo. Human clotting **factor VIII** cDNA with B-domain deleted was inserted into vector pRC/RSV to form pRC/RSV- hF VIII BD, which conjugated with in vivo **liposome** transfection

reagent(DOTAP-Cholesterol) to accomplish a kind of **therapeutic** gene, pRC/RSV-hF VIII BD-DOTAP-Cholesterol. Mice were injected with pRC/RSV-hF VIII BD-DOTAP-Cholesterol i.m. and sacrificed 48 h, 10 days, 20 days, 30 days, 40 days and 50 days later, resp. Tissues such as heart, liver, spleen, lung, kidney and muscle were harvested, the distribution and transcription as well as expression of hF VIII BD cDNA were detected by means of PCR, RT-PCR and immunohistochem. techniques. In addn., the antigen and antibody of hF VIII in plasma were measured. There was high expression of hF VIII in plasma and tissues at the 48th hour after injection. On day 10, antigen level of hF VIII in plasma reached its peak, 17.55 ng/mL, and gradually reduced later. The antibody of hF VIII in plasma emerged on day 10 after injection, and increased and gradually reached 37.06 U/mL on day 50 after injection. PCR, RT-PCR and immunohistochem. showed that hF VIII BD cDNA and its transcription as well as expression existed in all kinds of tissues, and lasted longer in spleen, lungs and kidneys than in heart, liver and muscle. **Therapeutic** gene, pRC/RSV-hF VIII BD-DOTAP-Cholesterol, produced by combination of pRC/RSV-hF VIII BD and DOTAP-Cholesterol **liposome** can express human F VIII successfully in vivo, which lays an exptl. foundation for curing **hemophilia** A by gene-**drug** in clinic.

L29 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:293982 HCAPLUS
DOCUMENT NUMBER: 136:291348
TITLE: Xenogeneic antibody containing plasma reagents and associated methods
INVENTOR(S): Turecek, Peter; Schwarz, Hans-Peter; Gritsch, Herbert
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Austria
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002031515	A2	20020418	WO 2001-EP11310	20011001

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-687823 A 20001013

AB A bioassay reagent is provided consisting of a xenogeneic antibody contg. plasma. Specifically, the bioassay reagent disclosed contains plasma from a first animal species and antibodies derived from at least one second different animal species that recognize antigens indigenous to the first animal species. More specifically, a bioassay for assessing the efficacy

of **therapeutics** intended to treat patients having autoimmune diseases, specifically, **hemophiliacs** having anti-blood factor antibodies (inhibitory factors) present in their blood. Also provided are assocd. methods for making and using the bioassay reagents disclosed.

IT **9001-27-8**, Blood-coagulation **factor VIII**
109319-16-6
RL: ANT (Analyte); ANST (Analytical study)
(xenogeneic antibody contg. plasma reagents and assocd. methods)

L29 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:730971 HCAPLUS
DOCUMENT NUMBER: 135:299500
TITLE: Gene therapy by targeted mutation using single stranded oligonucleotides with modified backbones
INVENTOR(S): Kmiec, Eric B.; Gamper, Howard B.; Rice, Michael C.
PATENT ASSIGNEE(S): University of Delaware, USA
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073002	A2	20011004	WO 2001-US9761	20010327

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-192176P P 20000327
US 2000-192179P P 20000327
US 2000-208538P P 20000601
US 2000-244989P P 20001030

AB Presented are methods and compns. for targeted mutation of a chromosomal site using modified single-stranded oligonucleotides. The oligonucleotides of the invention have at least one modified nucleotide. The oligonucleotides of the invention have at least one modified nuclease-resistant terminal region comprising phophorothioate linkages, LNA analogs or 2'-O-Me base analogs. The oligonucleotides can enter cells where they will hybridize with a target sequence leading to formation of a mismatched heteroduplex that will be cor. by DNA repair mechanisms.

L29 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:300514 HCAPLUS
DOCUMENT NUMBER: 134:331617
TITLE: Oil-in-water emulsion compositions for polyfunctional active ingredients
INVENTOR(S): Chen, Feng-jing; Patel, Mahesh V.

PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028555	A1	20010426	WO 2000-US28835	20001018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002107265	A1	20020808	US 1999-420159	19991018

PRIORITY APPLN. INFO.: US 1999-420159 A 19991018

AB **Pharmaceutical** oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aq. phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the **pharmaceutical** emulsions. For example, an emulsion was prepd., with cyclosporin A as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The compn. contained (by wt.) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

IT **113189-02-9**, **Antihemophilic** factor
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oil-in-water emulsion compns. for polyfunctional active ingredients)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:136991 HCAPLUS
DOCUMENT NUMBER: 134:198075
TITLE: Triglyceride-free compositions and methods for enhanced absorption of hydrophilic **therapeutic** agents
INVENTOR(S): Patel, Mahesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309663	B1	20011030	US 1999-375636	19990817
EP 1210063	A1	20020605	EP 2000-947184	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2001024658	A1	20010927	US 2000-751968	20001229

PRIORITY APPLN. INFO.: US 1999-375636 A 19990817
WO 2000-US18807 W 20000710

AB The present invention relates to triglyceride-free **pharmaceutical** compns., **pharmaceutical** systems, and methods for enhanced absorption of hydrophilic **therapeutic** agents. The compns. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic **therapeutic** agent can be incorporated into the compn., or can be co-administered with the compn. as part of a **pharmaceutical** system. The invention also provides methods of treatment with hydrophilic **therapeutic** agents using these compns. and systems. For example, when a compn. contg. Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. **drug** was enhanced by 991%.

IT **113189-02-9, Antihemophilic** factor
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. for enhanced absorption of hydrophilic **drugs** using combination of surfactants)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:634348 HCAPLUS
DOCUMENT NUMBER: 134:315946
TITLE: Highly purified human **factor VIII**: concentrate prepared by ion-exchange chromatography
AUTHOR(S): Luo, Liang; Yuan, Jin; Mu, Lei
CORPORATE SOURCE: Chengdu Inst. of Biological Products, Chengdu, 610063, Peop. Rep. China
SOURCE: Huaxi Yaoxue Zazhi (2000), 15(3), 174-176

CODEN: HYZAE2; ISSN: 1006-0103
PUBLISHER: Huaxi Yike Daxue Yaoxueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A new ion-exchange chromatog. procedure for prepg. a highly purified **factor VIII** conc. from plasma cryoppt. was presented. The process comprised dissolving a cryoppt. in Na heparinate soln., regulating with HCl to pH 6.2, cooling to 15.degree., pptg. with PEG, concg., regulating supernatant liquor with NaOH to pH 7.0, adding S/D reagent, 1% Tween-80, and 0.3% tri-Bu phosphate, standing at 25.degree. for >8 h to inactivate **lipid**-enveloped viruses, purifying on a DEAE-Fractogel TSK 650M column, eluting with 0.15M NaCl buffer to remove protein impurities, eluting with 0.25M NaCl buffer, and filtering sterilized or adding a protein stabilizer. The chromatog. recovery of **FVIII** was 70-90%, and the specific activity of FVII was >100 IU mg-1 compared with a purifn. factor of over 5000 from plasma. The conc. with high purity may be well tolerated and effective in clin. treatment of **hemophilia** A patients.

IT **113189-02-9P, Factor VIII**
RL: PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly purified human **factor VIII** conc. prepd. by ion-exchange chromatog.)

L29 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456817 HCAPLUS
DOCUMENT NUMBER: 133:84273
TITLE: Methods for reducing adverse side effects associated with transplantation of cells expressing tissue factor
INVENTOR(S): Hurwitz, David R.; Cherington, Van; Galanopoulos, Theofanis; Levine, Peter H.; Greenberger, Joel S.
PATENT ASSIGNEE(S): Alg Co., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038517	A1	20000706	WO 1999-US31080	19991228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6387366	B1	20020514	US 1998-224048	19981231
EP 1143797	A1	20011017	EP 1999-966696	19991228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1998-224048 A1 19981231
WO 1999-US31080 W 19991228

AB The methods of the present invention are based on the discovery that adverse side effects (such as hemorrhage) can occur upon infusion of cells that express tissue factor. Accordingly, the methods of the invention are aimed at reducing the biol. activity of tissue factor (TF) in a patient, and can be carried out by, for example: infusing fewer cells (or infuse the same no. of BMSCs over a longer period of time); reducing the expression or activity of TF (within the infused cells specifically) (e.g., by contacting the cells with a TF antagonist in vitro) or within the patient generally (e.g., by administering a TF antagonist to the patient); hampering the interaction of TF with factor VII(a); inhibiting the activity of the TF-factor VII(a) complex once it has formed; or inhibiting the coagulation cascade at any point downstream from formation of the complex (including inhibition of platelet activation).

IT **113189-02-9**, Blood coagulation **factor viii**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(deficiency; methods for reducing adverse side effects assocd. with transplantation of cells expressing tissue factor)

IT **9013-93-8**, Phospholipase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for reducing adverse side effects assocd. with transplantation of cells expressing tissue factor)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:257388 HCAPLUS
DOCUMENT NUMBER: 133:286298
TITLE: Pasteurized, monoclonal antibody **factor VIII** concentrate: establishing a new standard for purity and viral safety of plasma-derived concentrates
AUTHOR(S): Goldsmith, J. C.
CORPORATE SOURCE: Centeon L.L.C., King of Prussia, PA, 19406, USA
SOURCE: Blood Coagulation & Fibrinolysis (2000), 11(2), 203-215
CODEN: BLFIE7; ISSN: 0957-5235
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A **factor VIII** conc. (Monoclate-P) manufd. using a combination of pasteurization and immunoaffinity chromatog. has been chosen to compare and contrast manufg. aspects of plasma-derived **factor VIII** concs. Pasteurization is a virucidal method with a long safety record in clin. practice, while immuno-affinity chromatog. selectively isolates and purifies the procoagulant protein of **factor VIII**, and partitions potential viral contaminants and nonessential proteins to the unbound fraction. The complete Monoclate-P prodn. process reduces human immunodeficiency virus by

.gtoreq. 10.5 log10, Sindbis (a model for hepatitis C virus) by .gtoreq. 6.5 log10, and murine encephalomyocarditis virus (a non-enveloped model virus) by 7.1 log10. The viral safety of Monoclate-P has been further demonstrated in clin. studies in patients not previously treated with blood or plasma-derived products. Addnl., the manuf. of Monoclate-P includes careful donor screening and plasma testing for antibodies to syphilis and human immunodeficiency, hepatitis B, and hepatitis C viruses to enhance source plasma safety. Combined with donor selection and plasma testing, multiple viral redn. steps effectively eliminate both **lipid**-enveloped viruses (e.g. human immunodeficiency, hepatitis B and C) and non-**lipid**-enveloped viruses (e.g. hepatitis A). In addn., polymerase chain reaction-based nucleic acid detection tests for hepatitis B and C viruses and for human immunodeficiency virus-1 have been introduced as part of an investigational new **drug** mechanism.

IT **113189-02-9P**, **Antihemophilic** factor
RL: ADV (Adverse effect, including toxicity); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pasteurization and immunoaffinity chromatog. for prepn. of monoclonal antibody **factor VIII** as std. for purity and viral safety of plasma-derived concs.)

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15227 HCAPLUS
DOCUMENT NUMBER: 132:77836
TITLE: Improved process for preparing Schiff base adducts of amines with o-hydroxy aldehydes and compositions of matter based thereon
INVENTOR(S): Hay, Bruce Allan; Clark, Michael Thomas
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000507	A1	20000106	WO 1999-IB993	19990602
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9938424	A1	20000117	AU 1999-38424	19990602
EP 1087989	A1	20010404	EP 1999-921066	19990602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				

SI, LT, LV, FI, RO

BR 9912203	A	20010410	BR 1999-12203		19990602
JP 2002519356	T2	20020702	JP 2000-557268		19990602
PRIORITY APPLN. INFO.:			US 1998-90714P	P	19980626
			US 1998-90714	P	19980626
			WO 1999-IB993	W	19990602

OTHER SOURCE(S): MARPAT 132:77836

AB An improved process is described for prepg. Schiff base condensation adduct final products whose components comprise a protein having beneficial activity in animals, and an arom. o-hydroxy aldehyde, which comprises bringing together the above-mentioned components in an aq. environment at a pH of 7.0 or higher to form a reaction mixt., under conditions effective to drive said condensation reaction substantially to completion by removing from about 97.0 % to about 99.9 % by wt., preferably from about 98.0 % to about 99.0 % by wt. of the water already present or produced during said condensation reaction, consistent with maintaining the integrity of the condensation reactants and adduct final product, and to assure a rate of conversion to said condensation adduct final product, i.e. , with resulting yield of said condensation adduct final product of equal to or greater than about 98.5 % by wt., preferably equal to or greater than about 99.5 % by wt. based on the wt. of the reactants. Preferred arom. o-hydroxy aldehydes comprise o-vanillin; salicylaldehyde; 2,3-dihydroxybenzaldehyde; 2,6-dihydroxybenzaldehyde; 2-hydroxy-3-ethoxybenzaldehyde; or pyridoxal. A very wide range of proteins may be employed. The improved process provides yields over 90 % and substantially quant. conversion of the aldehyde and protein to the condensation adduct.

IT **65154-06-5**, PAF **113189-02-9**, **Antihemophilic** factor
RL: FFD (Food or feed use); RCT (Reactant); **THU (Therapeutic use)** ; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(improved process for prepg. Schiff base adducts of peptide and protein amine groups with o-hydroxy aldehydes and compns. based thereon for food and **drug** use)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:337391 HCAPLUS
DOCUMENT NUMBER: 127:39587
TITLE: Transmission of parvovirus B19 by coagulation factor concentrates exposed to 100.degree.C heat after lyophilization
AUTHOR(S): Santagostino, E.; Mannucci, P.M.; Gringeri, A.; Azzi, A.; Morfini, M.; Musso, R.; Santoro, R.; Schiavoni, M.
CORPORATE SOURCE: Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Maggiore Hospital and the University of Milan, Milan, Italy
SOURCE: Transfusion (Bethesda, Maryland) (1997), 37(5), 517-522
CODEN: TRANAT; ISSN: 0041-1132
PUBLISHER: American Association of Blood Banks
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Double inactivation by solvent/detergent treatment plus heating at 100.degree.C for 30 min after lyophilization has been adopted to improve viral safety of **factor VIII** and factor IX concs., particularly with respect to non-**lipid**-enveloped viruses. The aim of this study was to evaluate the safety of concs. exposed to these virucidal methods. None of the 26 patients seroconverted for human immunodeficiency virus or hepatitis C virus. Hepatitis B virus markers remained neg. in the 10 unvaccinated **hemophiliacs**. No hepatitis A virus seroconversion occurred among 17 susceptible patients. B19 seroconversion (IgM) and B19 viremia were obsd. within 2 wk of the first conc. infusion in 8 of 15 susceptible patients, 5 of 11 treated with **factor VIII** and 3 of 4 with factor IX conc. This prospective study indicates that very high temps. applied to lyophilized concs. appear to prevent the transmission of hepatitis A virus to **hemophiliacs**. However, B19 parvovirus still contaminates concs. despite the use of this robust virucidal method.
IT **9001-27-8**, Blood coagulation **factor VIII**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(transmission of parvovirus B19 by coagulation factor concs. exposed to 100.degree.C heat after lyophilization)

L29 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:264330 HCAPLUS
DOCUMENT NUMBER: 126:311993
TITLE: Transfection of the human heme oxygenase gene into rabbit coronary microvessel endothelial cells: protective effect against heme and hemoglobin toxicity
AUTHOR(S): Abraham, N. G.
CORPORATE SOURCE: The Rockefeller University, New York, NY, 10021, USA
SOURCE: Molecular Biology of Hematopoiesis 5, [Proceedings of the Symposium on the Molecular Biology of Hematopoiesis], 9th, Genoa, June23- 27, 1995 (1996), Meeting Date 1995, 351-360. Editor(s): Abraham, Nader G. Plenum: New York, N. Y.
CODEN: 64GMAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Heme oxygenase* (HO) is a stress protein and has been suggested to participate in defense mechanisms against agents which may induce oxidative injury such as metals, endotoxin, heme-Hb and various cytokines. Overexpression of HO in cells might therefore protect against oxidative stress produced by certain of these agents, specifically heme and Hb, by catalyzing their degrdn. to bilirubin, which itself has anti-oxidant properties. We report here the successful in vitro transfection of rabbit coronary microvessel endothelial cells with a functioning gene encoding the human HO enzyme. A plasmid contg. the cytomegalovirus promoter and the human HO cDNA complexed to cationic **liposomes** (Lipofectin) was used to transfect rabbit endothelial cells. Cells transfected with human HO exhibited a .apprxeq.3.0-fold increase in enzyme activity and expressed a several-fold induction of human HO mRNA as compared to

endogenous rabbit HO mRNA. Transfected and non-transfected cells expressed **Factor VIII** antigen and exhibited similar acetylated low d. lipoprotein uptake (two important features which characterize endothelial cells) with greater than 85% of cells staining pos. for each marker. Moreover, cells transfected with the human HO gene acquired substantial resistance to toxicity produced by exposure to recombinant Hb (rHb) and heme as compared to non-transfected cells. The protective effect of HO overexpression against heme/Hb toxicity in endothelial cells shown in these studies provides direct evidence that the inductive response of human HO to such injurious stimuli represents an important tissue adaptive mechanism for moderating the severity of cell damage produced by these blood components.

IT **113189-02-9, Antihemophilic** factor
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transfection of the human heme oxygenase gene into rabbit coronary microvessel endothelial cells: protective effect against heme and Hb toxicity)

L29 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:113413 HCAPLUS
DOCUMENT NUMBER: 126:114823
TITLE: Crosslinkable polypeptide compositions and their use in delivery of biologically active agents to subjects
INVENTOR(S): Sojomihardjo, Soebianto A.; Desai, Neil P.; Sandford, Paul A.; Soon-shiong, Patrick; Nagrani, Shubhi
PATENT ASSIGNEE(S): Vivorx Pharmaceuticals, Inc., USA; Sojomihardjo, Soebianto, A.; Desai, Neil, P.; Sandford, Paul, A.; Soon-Shiong, Patrick; Nagrani, Shubhi
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640829	A1	19961219	WO 1996-US7424	19960521
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9658012	A1	19961230	AU 1996-58012	19960521

PRIORITY APPLN. INFO.: US 1995-484724 19950607
WO 1996-US7424 19960521

AB In accordance with the present invention, there are provided rapidly crosslinkable polypeptides which are obtained upon introduction of unsatd. group(s) into the polypeptide via linkage to amino acid residues on the polypeptide directly through one of three types of linkages, namely, an amide linkage, an ester linkage, or a thioester linkage. Each of these linkages are obtainable in a single step by use of a single derivatizing

agent, acrylic anhydride. Also provided are methods for prepg. such modified polypeptides and various uses therefor. It has unexpectedly been found that proteins with the above-described chem. modifications have the ability to rapidly crosslink to themselves under suitable conditions. This crosslinking occurs in the absence of any external crosslinking agents (indeed, in the absence of any extraneous agents), resulting in the formation of a solid gel material. Solid crosslinked gels are formed in seconds, starting from a freely flowing soln. of polypeptide. Applications of such materials are broad ranging, including the encapsulation of living cells, the encapsulation of biol. ative materials, the in situ formation of degradable gels, the formation of wound dressings, the prevention of post-surgical adhesions, gene delivery, **drug** targetting, as a microcarrier for culture of living cells, and the like. Albumin was reacted with acrylic anhydride to produce a photopolymerizable albumin deriv. A soln. of this deriv., insulin, a free radical initiator (ethyl eosin), a cocatalyst (triethanolamine), and an accelerator (vinyl pyrrolidinone) was irradiated with an Hg lamp to encapsulate the insulin. Diabetic rats were injected with the encapsulated insulin. This compn. was able to maintain lower blood sugar for a longer period of time than the control, com. injectable insulin.

IT **9001-62-1DP**, Lipase, derivs. **113189-02-9DP**, **Factor VIII**, derivs.
RL: BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(unsatd. group-contg.; crosslinkable polypeptide compns. and their use in delivery of biol. active agents to subjects)

L29 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:469700 HCAPLUS
DOCUMENT NUMBER: 125:123695
TITLE: Solubilization aids for hydrophilic macromolecules
INVENTOR(S): New, Roger Randal Charles; Kirby, Christopher John
PATENT ASSIGNEE(S): Cortecs Limited, UK
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9617593	A1	19960613	WO 1995-GB2891	19951208
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2207279	AA	19960613	CA 1995-2207279	19951208
AU 9641224	A1	19960626	AU 1996-41224	19951208
EP 796085	A1	19970924	EP 1995-939369	19951208

EP 796085 B1 20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
CN 1169113 A 19971231 CN 1995-196700 19951208
JP 10510256 T2 19981006 JP 1995-517436 19951208
AT 192920 E 20000615 AT 1995-939369 19951208
ZA 9510508 A 19970611 ZA 1995-10508 19951211
NO 9702608 A 19970808 NO 1997-2608 19970606
US 5968549 A 19991019 US 1997-870516 19970606
FI 9702442 A 19970609 FI 1997-2442 19970609
PRIORITY APPLN. INFO.: GB 1994-24902 A 19941209
WO 1995-GB2891 W 19951208

AB The invention provides a process for the prepn. of a single phase hydrophobic prepn. comprising a hydrophilic species in a hydrophobic solvent wherein a compd. which is: (a) a low-mol. wt. compd. having at least some degree of polarity; and/or (b) a **lipid**-sol. org. acid; and/or (c) a amphiphile; and (d) glycerol or other polyhydric alcs.; is added during the process to aid solubilization. Solubilization of hydrophilic species (e.g. aprotinin) in a hydrophobic solvent (e.g. sunflower oil) is useful in **pharmaceutical** industry, food technol., or cosmetic industry.

IT **113189-02-9, Antihemophilic** factor
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(agents for solubilization of hydrophilic macromols. in hydrophobic solvents)

L29 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:972824 HCAPLUS
DOCUMENT NUMBER: 124:97355
TITLE: Virucidal short wavelength ultraviolet light treatment of plasma and **factor VIII** concentrate: protection of proteins by antioxidants
AUTHOR(S): Chin, Sing; Williams, Bolanle; Gottlieb, Paul; Margolis-Nunno, Henrietta; Ben-Hur, Ehud; Hamman, John; Jin, Rongyu; Dubovi, Edward; Horowitz, Bernard
CORPORATE SOURCE: New York Blood Cent., Cornell Univ., Ithaca, NY, USA
SOURCE: Blood (1995), 86(11), 4331-6
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of solvent/detergent mixts. and various forms of heat treatment to inactivate viruses has become widespread in the prepn. of blood derivs. Because viruses that lack **lipid** envelopes and/or are heat resistant, e.g., hepatitis A virus (HAV) or parvovirus B19 may be present, the use of two methods of virus elimination that operate by different mechanisms has been advocated. The authors now report on short wavelength UV light (UVC) irradn. for virus inactivation and enhancement of its compatibility with proteins by quenchers of reactive oxygen species (ROS). Treatment of an **antihemophilic** factor (AHF) conc. or whole plasma with 0.1 J/cm2 inactivated 105 to .gtoreq.106 infectious doses (ID) of encephalomyocarditis virus (EMCV), HAV, bacteriophage M13, vesicular stomatitis virus (VSV), and porcine parvovirus. However, the recovery of

factor VIII was 30% or lower on treatment of an AHF conc. and 60% on treatment of plasma. **Factor VIII** recovery could be increased with little or no effect on virus kill by addn. of rutin, a flavonoid known to quench both type I and type II ROS. On treatment of plasma in the presence of rutin, the recovery of several other coagulation factors was also enhanced by rutin addn. and typically exceeded 75%. Electrophoretic anal. of treated AHF conc. confirmed the advantage of rutin presence; UVC irradn. of plasma did not cause discernible changes in electrophoretic banding patterns, even in the absence of rutin. The authors conclude that addn. of UVC treatment to existing processes used in the manuf. of blood derivs. will provide an added margin of safety, esp. for nonenveloped or heat-stable viruses.

IT **113189-02-9, Antihemophilic** factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(virucidal UVC treatment of plasma and **factor VIII** conc. in relation to the protection of proteins by antioxidants)

L29 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:746373 HCAPLUS
DOCUMENT NUMBER: 123:123218
TITLE: Hydrophobic preparations of hydrophilic compounds
INVENTOR(S): New, Roger Randal Charles; Kirby, Christopher John
PATENT ASSIGNEE(S): Cortecs Ltd., UK
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513795	A1	19950526	WO 1994-GB2495	19941114
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2176577	AA	19950526	CA 1994-2176577	19941114
AU 9481496	A1	19950606	AU 1994-81496	19941114
AU 689509	B2	19980402		
EP 729350	A1	19960904	EP 1995-900838	19941114
EP 729350	B1	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1137751	A	19961211	CN 1994-194506	19941114
JP 11514328	T2	19991207	JP 1994-514287	19941114
AT 199494	E	20010315	AT 1995-900838	19941114
ES 2154719	T3	20010416	ES 1995-900838	19941114
ZA 9409109	A	19960516	ZA 1994-9109	19941116
US 6368619	B1	20020409	US 1996-648065	19960515

PRIORITY APPLN. INFO.: GB 1993-23588 A 19931116
WO 1994-GB2495 W 19941114

AB Single phase prepns. of hydrophilic species, in particular macromol. compds. such as proteins or glycoproteins in a hydrophobic solvent such as an oil can be obtained by prepg. a hydrophile/amphiphile array in which the hydrophilic head groups of the amphiphile are oriented towards the hydrophilic species and bringing the array into contact with the hydrophobic solvent. The prepns. of the invention can be used alone or can be combined with an aq. phase to form emulsions in which the hydrophilic species is present in the hydrophobic phase. The compns. of the present invention are versatile and have application in the **pharmaceutical**, food, cosmetic, chem. and agricultural industries.

IT **2644-64-6**, Dipalmitoylphosphatidylcholine **9001-62-1**, Lipase **113189-02-9**, **Antihemophilic** factor
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(hydrophobic compns. for hydrophilic compds.)

L29 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:309109 HCAPLUS
DOCUMENT NUMBER: 122:72036
TITLE: Use of platelet-activating factor (PAF) to increase the levels of von Willebrand factor (vWF) and/or **Factor VIII** in blood
INVENTOR(S): Hashemi, Sofia; Palmer, Douglas
PATENT ASSIGNEE(S): Canadian Red Cross Society (the), Can.
SOURCE: Can. Pat. Appl., 34 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2090738	AA	19940825	CA 1993-2090738	19930224
CA 2090738	C	19960521		
US 5631246	A	19970520	US 1993-31573	19930315

PRIORITY APPLN. INFO.: CA 1993-2090738 19930224

AB PAF and its analogs are particularly useful in the treatment of von Willebrand disease and **hemophilia** A for increasing the levels of vWF and/or **Factor VIII** in the blood. Thus, (1-deamino-8-D-arginine)vasopressin induced PAF secretion by monocytes; the monocyte supernatant, or purified PAF, caused human umbilical vein endothelial cells to release vWF and PGI2.

IT **65154-06-5**, Blood platelet-activating factor **65154-06-5D**, Blood platelet-activating factor, derivs.
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of platelet-activating factor (PAF) to increase levels of von Willebrand factor and **Factor VIII** in blood)

IT **9001-27-8**, Blood-coagulation **factor VIII**, complex **109319-16-6**, Blood-coagulation **factor VIII**, von Willebrand's
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(use of platelet-activating factor (PAF) to increase levels of von Willebrand factor and **Factor VIII** in blood)

L29 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:566440 HCAPLUS
DOCUMENT NUMBER: 115:166440
TITLE: Evaluation of wet pasteurization of a **factor VIII** concentrate produced by controlled-pore silica adsorption
AUTHOR(S): Hiemstra, H.; Nieuweboer, Carina E. F.; Idoe, M. A.; Claassen, Jolien E.; Vos, Aster H. V.; Tersmette, M.; Strengers, P. F. W.; Over, J.; Mauser-Bunschoten, Eveline P.; et al.
CORPORATE SOURCE: Cent. Lab., Neth. Red Cross Blood Transfus. Serv., Amsterdam, NL-1006 AD, Neth.
SOURCE: Folia Haematol. (Leipzig) (1990), 117(4), 557-63
CODEN: FOHEAW; ISSN: 0323-4347
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the routine prodn. of a **factor VIII** (I) conc. (produced by the adsorption of contaminating proteins in cryoppts. on to controlled-pore SiO2 and concn. of the effluent by ultrafiltration), the terminal dry-heat treatment (72 h at 60.degree.) was replaced by pasteurization (10-11 h at 60.degree.) in the liq. state. High effectivity of this procedure with respect to virus inactivation was demonstrated with a variety of both **lipid**- protein-enveloped model viruses, including HIV. Pair-wise quality control of dry-heated and pasteurized product revealed no differences, except in the compn. of the formulation buffer. A clin. study with **hemophilia** A patients showed the pasteurized product was well tolerated and the in vivo recovery and half-life of I were in the same (normal) range as found for the dry-heated counterpart.
IT **9001-27-8**, Blood coagulation **factor VIII**
RL: BIOL (Biological study)
(conc., hepatitis non-A non-B deactivation in, pasteurization vs.; dry heating for, model study of)

L29 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:504429 HCAPLUS
DOCUMENT NUMBER: 109:104429
TITLE: **Factor VIII**-bypassing activity of bovine tissue factor using the canine **hemophilic** model
AUTHOR(S): O'Brien, Donogh P.; Giles, Alan R.; Tate, Keri M.; Vehar, Gordon A.
CORPORATE SOURCE: Dep. Cardiovasc. Res., Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: J. Clin. Invest. (1988), 82(1), 206-11
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hemophilia** A, currently treated by replacement **therapy** of **factor VIII**, is frequently complicated by the development of neutralizing antibodies. The **therapeutic** potential of attenuated forms of the **lipid**-assocd. glycoprotein tissue factor, a known initiator of coagulation, was investigated as a

factor VIII-bypassing activity. The protein moiety of tissue factor (Apo-TF) was partially purified and exhibited min. procoagulant activity before relipidation in vitro. In pilot studies, Apo-TF injection into rabbits previously anticoagulated with an antibody to **factor VIII** had a procoagulant effect. The efficacy of the material was further demonstrated when injection of Apo-TF in **hemophilic** dogs resulted in a normalization of the cuticle bleeding time. Little or no change in the blood parameters assocd. with disseminated intravascular coagulation was obsd. at lower doses, although mild to moderate effects were seen at higher doses. These data suggest a novel role for Apoo-TF prepns. as a potential **therapeutic** agent for **hemophiliacs** with antibodies to **factor VIII** once the potential thrombogenicity of such materials is evaluated.

IT **113189-02-9**, Blood-coagulation **factor VIII**
RL: BIOL (Biological study)
(antibodies to, protein moiety of tissue factor in **hemophilia** A treatment in relation to)

L29 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:118954 HCAPLUS
DOCUMENT NUMBER: 108:118954
TITLE: Removal of **lipid** soluble process chemicals from biological materials by extraction with naturally occurring oils or synthetic substitutes thereof
INVENTOR(S): Woods, Kenneth R.; Orme, Thomas W.
PATENT ASSIGNEE(S): New York Blood Center, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 239859	A2	19871007	EP 1987-103821	19870317
EP 239859	A3	19880622		
EP 239859	B1	19980128		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
US 4789545	A	19881206	US 1986-846374	19860331
ZA 8700885	A	19870930	ZA 1987-885	19870206
AT 162798	E	19980215	AT 1987-103821	19870317
ES 2112239	T3	19980401	ES 1987-103821	19870317
JP 62240623	A2	19871021	JP 1987-79540	19870331
JP 2544619	B2	19961016		
JP 08268898	A2	19961015	JP 1996-26897	19960214

PRIORITY APPLN. INFO.: US 1986-846374 19860331

AB **Lipid**-sol. process chems. are removed, e.g. in virus-free physiol. acceptable plasma prodn., by extn. with a natural plant or animal oil or a synthetic compd. of similar structure. Aq. **antihemophilic** factor conc. contg. tri-Bu phosphate was extd. 3 times with soybean oil at 5, 10, or 20% by vol.; all 3 levels of soybean oil gave essentially 100% extn. by the end of the 3rd extn. In another

example, Tween 80 was poorly (.apprx.20%) extd., but other commonly used detergents were >80% extd. by soybean oil.

IT **113189-02-9P**
RL: PUR (Purification or recovery); PREP (Preparation)
(conc., **lipid**-sol. process chems. removal from, oils and synthetic triglycerides for)

L29 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:174446 HCAPLUS
DOCUMENT NUMBER: 104:174446
TITLE: Use of **lipid** solvents for viral inactivation in **factor VIII** concentrates
AUTHOR(S): Mitra, G.; Wong, M.
CORPORATE SOURCE: Biol. Res. Dev., Cutter Lab., Berkeley, CA, 94710, USA
SOURCE: Biotechnol. Bioeng. (1986), 28(2), 297-300
CODEN: BIBIAU; ISSN: 0006-3592
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Model virus inactivation studies with **lipid** solvents were carried out in **antihemophilic** factor [**9001-27-8**] concs. The procoagulant activity obtained was .gtoreq.80% recovery with 20% amyl acetate [628-63-7]-0.1% deoxycholate [83-44-3]. A concurrent redn. of 4 logs of virus titer was obtained for model viruses provided the viral mass contained significant amts. (>20%) of **lipid**. From this preliminary study it appears that further investigations in animal models may be warranted to demonstrate the inactivation of hepatitis B virus, non-A-non-B virus, and AIDS virus with 20% amyl acetate-0.1% deoxycholate in **antihemophilic** factor concs.

IT **9001-27-8**
RL: BIOL (Biological study)
(viruses in, **lipid** solvents inactivation of)

L29 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:56264 HCAPLUS
DOCUMENT NUMBER: 104:56264
TITLE: Inactivation of viruses in labile blood derivatives. I. Disruption of **lipid**-enveloped viruses by tri(n-butyl)phosphate detergent combinations
AUTHOR(S): Horowitz, B.; Wiebe, M. E.; Lippin, A.; Stryker, M. H.
CORPORATE SOURCE: New York Blood Cent., New York, NY, USA
SOURCE: Transfusion (Philadelphia) (1985), 25(6), 516-22
CODEN: TRANAT; ISSN: 0041-1132
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Use of the org. solvent, tributyl phosphate (TNBP) [126-73-8], and detergents for the inactivation of viruses in labile blood derivs. was evaluated by addn. of marker viruses (VSV, Sindbis, Sendai, EMC) to **antihemophilic** factor (AHF) [**9001-27-8**] concs. The rate of virus inactivation obtained with TNBP plus Tween 80 [9005-65-6] was superior to that obsd. with Et2O plus Tween 80, a condition previously shown to inactivate greater than or equal to 106.9 CID50 of hepatitis B and greater than or equal to 104 CID50 of Hutchinson strain non-A, non-B hepatitis. The AHF recovery after TNBP/Tween treatment was greater than or equal to 90%. Following the reaction, TNBP could be removed from the

protein by gel exclusion chromatog. on Sephadex G25; however, because of its large micelle size, Tween 80 could not be removed from protein by this method. Attempts to remove Tween 80 by differential preferentiation of protein were only partially successful. An alternate detergent, Na cholate [361-09-1], when combined with TNBP, resulted in almost as efficient virus inactivation and an 80% recovery of AHF. Because Na cholate forms small micelles, it could be removed by Sephadex G25 chromatog. Electrophoretic examn. of TNBP/cholate-treated AHF concs. revealed few, if any, changes in protein mobility, except for plasma lipoprotein(s).

IT **9001-27-8**
RL: BIOL (Biological study)
(virus inactivation in, by tri-Bu phosphate-detergent combinations)

L29 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:137785 HCAPLUS
DOCUMENT NUMBER: 102:137785
TITLE: Undenatured virus-free biologically active protein derivatives
INVENTOR(S): Neurath, Alexander Robert; Horowitz, Bernhard
PATENT ASSIGNEE(S): New York Blood Center, USA
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 131740	A2	19850123	EP 1984-106557	19840608
EP 131740	A3	19850807		
EP 131740	B1	19901031		
EP 131740	B2	19940928		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4540573	A	19850910	US 1983-514375	19830714
AT 57836	E	19901115	AT 1984-106557	19840608
ZA 8404596	A	19850227	ZA 1984-4596	19840618
CA 1221910	A1	19870519	CA 1984-458166	19840705
AU 8430503	A1	19850117	AU 1984-30503	19840711
AU 563925	B2	19870730		
JP 60051116	A2	19850322	JP 1984-143386	19840712
JP 06102627	B4	19941214		
US 4764369	A	19880816	US 1984-631675	19840717
US 4820805	A	19890411	US 1985-726200	19850422

PRIORITY APPLN. INFO.:		
US 1983-514375		19830714
EP 1984-106557		19840608
US 1984-631675		19840717

AB Hepatitis and **lipid**-coated viruses were removed from blood protein-contg. compns. (e.g., whole blood, serum, plasma, etc.) with the protein activity of total protein being .gtoreq.80%. The protein-contg. compn. was contacted with di- or trialkyl phosphate, preferably a mixt. of trialkyl phosphate and detergent, usually followed by removal of the di- or trialkyl phosphate. E.g., compns. contg. **antihemophilic**

factor (AHF) [**9001-27-8**], vesticular stomatitis virus (VSV), Sindbis virus, Sendai virus were contacted with aq. 1% tris(butyl) phosphate [126-73-8] and 1% Tween 80 [9005-65-6]. The virus inactivation was 4.7, 5.8, and 5.0 log for VSV, Sindbis virus, and Sendai virus, resp. The AHF yield was 86%.

IT **9001-27-8**
RL: BIOL (Biological study)
(blood compns. contg. trialkyl phosphates and detergents and, for virus removal)

L29 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:577524 HCAPLUS
DOCUMENT NUMBER: 101:177524
TITLE: Preparation of **liposomes** containing blood coagulation **factor VIII**
PATENT ASSIGNEE(S): Green Cross Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59116228	A2	19840705	JP 1982-228534	19821224

AB **Liposomes** contg. blood-coagulation **factor VIII** (I) [**9001-27-8**] are prepd. for treatment of diseases such as **hemophilia**. **Lipid** thin films are first prepd., suspended in a medium, aggregated by addn. of Ca ions, frozen, thawed, mixed with I and a chelating agent to form the **liposomes**. Thus, 25 g phosphatidylserines (soybean **lecithins**) were dissolved in 500 mL CHCl3, and dried under reduced pressure to form **lipid** films. The films were suspended in a 5 L 20 mM Tris buffer (pH 7.3) contg. 100 mM NaCl and 0.1 mM EDTA. The suspension was cooled and treated with ultrasound (350 W) at 0.degree., and with 100 mM CaCl2 until the final CaCl2 concn. became 20 mM. The suspension was incubated 1 h at 37.degree. to cause an aggregation of films, and centrifuged 10 min at 3500 rpm. The particles were isolated and frozen at -80.degree.. They were then thawed out, mixed with 1 L I soln. (50 units/mL), and heated up to 37.degree. to allow the particles to bind with I. Then, 100 mM EDTA at pH 7.0 was added to a concn. of 15 mM. The suspension was incubated 30 min at 37.degree., centrifuged 30 min at 35,000 rpm to collect the **liposomes** contg. 32 units I/mL.

IT **9001-27-8**
RL: BIOL (Biological study)
(**liposomes** contg., for **hemophilia** treatment)

L29 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:460085 HCAPLUS
DOCUMENT NUMBER: 101:60085
TITLE: Preparation of **liposomes** containing **Factor VIII** for oral treatment of **hemophilia**

AUTHOR(S): Kirby, Christopher J.; Gregoriadis, Gregory
CORPORATE SOURCE: Div. Clin. Sci., Clin. Res. Cent., Harrow, HA1 3UJ, UK
SOURCE: J. Microencapsulation (1984), 1(1), 33-45
CODEN: JOMIEF
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Different types of **liposomes** composed of a variety of **lipids** were compared for their ability to incorporate **Factor VIII** [**9001-27-8**] for oral **therapy** of **hemophilia**. Reverse evapn. **liposomes** (REV) composed of unsatd. phospholipids, allowed adequate levels of entrapment for administration to **hemophilic** dogs, but failed to promote entry of **Factor VIII** into the vasculature, possibly due to **liposome** breakdown and denaturation of **Factor VIII** within the gastrointestinal tract. A novel technique was therefore developed which made possible high-yield entrapment of **Factor VIII** in much more stable **liposomes** based on the satd. phospholipid, distearoylphosphatidylcholine [**4539-70-2**]. This new technique has a no. of other important features which make it an attractive method for the incorporation of a wide range of materials into **liposomes**.
IT **4539-70-2**
RL: BIOL (Biological study)
(**liposomes** contg., for encapsulation of **factor VIII**, for **hemophilia** treatment)
IT **9001-27-8**
RL: BIOL (Biological study)
(**liposomes** contg., for oral **hemophilia** treatment)

L29 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:180008 HCAPLUS
DOCUMENT NUMBER: 100:180008
TITLE: Oral administration of concentrated **factor VIII** or IX preparation
AUTHOR(S): Sakuragawa, Nobuo; Takahashi, Kaoru; Horikoshi, Isamu; Ueno, Masaharu
CORPORATE SOURCE: Cent. Clin. Lab., Toyama Med. Pharm. Univ., Toyama, 930-01, Japan
SOURCE: Acta Med. Biol. (Niigata) (1983), 31(1), 1-9
CODEN: AMBNAS; ISSN: 0567-7734
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oral administration of encapsulated **factor VIII** [**9001-27-8**] and aprotinin [9087-70-1] loader multilamellar **liposomes** to patients with moderate **hemophilia** and factor IX [9001-28-9] and aprotinin (similarly enclosed in **liposome**) to dogs increased the plasma levels of **factor VIII** by 2% and factor IX to **therapeutically** effective levels. Aprotinin helps in preventing the degrdn. of the coagulation factors in the digestive tract.
IT **9001-27-8**
RL: BIOL (Biological study)
(bioavailability and **hemophilia** treatment of, after oral

administration to humans and lab. animals)

L29 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:161782 HCAPLUS
DOCUMENT NUMBER: 100:161782
TITLE: Blood coagulation **factor VIII** incorporation into **liposomes**
PATENT ASSIGNEE(S): Green Cross Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59021625	A2	19840203	JP 1982-132791	19820728

AB For the prepn. of **liposomes** contg. blood coagulation **factor VIII** [**9001-27-8**], the fibrinogen contaminant of the **factor VIII** must be eliminated because it interferes with **liposome** formation. Thus, blood coagulation **factor VIII** was purified by Sephacryl S-400 column chromatog., mixed with flakes of egg yolk **lecithin**, cholesterol, and diacetyl phosphate, and treated with ultrasound to obtain **liposomes** for treatment of **hemophilia**.

IT **9001-27-8P**
RL: PREP (Preparation)
(fibrinogens removal from, for **liposome** manuf.)

L29 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:603208 HCAPLUS
DOCUMENT NUMBER: 97:203208
TITLE: Preparation of blood coagulation **factor VIII**
PATENT ASSIGNEE(S): Green Cross Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 57136526	A2	19820823	JP 1981-22688	19810217

AB blood coagulation **factor VIII** [**9001-27-8**] Is isolated from human blood plasma for the **therapy** of **hemophilia**. For example, human blood plasma was placed in a container in which the inner wall had been coated with soybean **lecithin**. Shaking of this container disintegrated the film, and the **liposomes** formed selectively adsorbed blood coagulation **factor VIII** from the plasma. The **liposomes** were isolated and dissolved in a pH 7 imidazole buffer contg. Triton

X-100. The soln. was fractionated by pptn. with polyethylene glycol and **factor VIII** was isolated. The recovery rate was 80%.

IT **9001-27-8**
RL: PROC (Process)
(sepn. of, from blood plasma by **lecithin liposome** uptake)

L29 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:588254 HCAPLUS
DOCUMENT NUMBER: 97:188254
TITLE: **Pharmaceutical** composition for oral administration containing coagulation **factor VIII** or IX
INVENTOR(S): Horikoshi, Isamu; Sakuragawa, Nobuo; Ueno, Masaharu; Takahashi, Kaoru
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd. , Japan
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4348384	A	19820907	US 1981-309269	19811007
JP 57070814	A2	19820501	JP 1980-144508	19801017
JP 03000366	B4	19910107		
JP 57179122	A2	19821104	JP 1981-65685	19810428
JP 03000851	B4	19910109		

PRIORITY APPLN. INFO.: JP 1980-144508 19801017
JP 1981-65685 19810428

AB An oral prepn. for the treatment of **hemophilia** A or B consists of blood coagulation **factor VIII** [**9001-27-8**] or factor IX [9001-28-9] and a protease inhibitor incorporated in **liposomes** and (or) encapsulated in enteric capsules. The product provides for absorption of the coagulation factor from the intestinal tract without significant decompn. Thus, **liposomes** were prepd. from egg yolk **lecithin** contg. 5% alc. phosphatidic acid and a pH 7 phosphate buffer soln. of **factor VIII** (3000 units); aprotinin [9087-70-1] was added and the **liposome** suspension was washed with NaCl soln., cooled, centrifuged, and the **liposomes** were dried. Intestinal capsules were packed with 10 mL **liposomes** contg. 1000 units of **factor VIII** and 17,000 units aprotinin to give 50 units of **factor VIII**/capsule.

IT **9001-27-8**
RL: BIOL (Biological study)
(enteric-encapsulated **liposomes** contg. aprotinin and, for oral **hemophilia** treatment)

L29 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:460998 HCAPLUS
DOCUMENT NUMBER: 97:60998
TITLE: **Pharmaceutical** composition for oral

administration containing coagulation **factor VIII**
INVENTOR(S): Horikoshi, Isamu; Sakuragawa, Nobuo; Ueno, Masaharu; Takahashi, Kaoru
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Fr. Demande, 14 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2492260	A1	19820423	FR 1981-19522	19811016
FR 2492260	B1	19840727		
JP 57070814	A2	19820501	JP 1980-144508	19801017
JP 03000366	B4	19910107		
GB 2085729	A	19820506	GB 1981-30122	19811006
GB 2085729	B2	19840418		
DE 3141223	A1	19820624	DE 1981-3141223	19811016
ES 506320	A1	19830516	ES 1981-506320	19811016

PRIORITY APPLN. INFO.: JP 1980-144508 19801017

AB An oral formulation for the treatment or prophylaxis of **hemophilia** A was prepd. comprising blood-coagulation **factor VIII** [**9001-27-8**] and a protease inhibitor incorporated into **liposomes** and eventually lyophilized and/or encapsulated in enterosol. capsules. Thus, a soln. of 2 g egg yolk **lecithin** and phosphatidic acids (5%) in 40 mL EtOH was concd. in vacuo to form a thin film and a soln. of 3000 units of **factor VIII** and 150,000 units aprotinin [9087-70-1] in phosphate buffer was added to form a **liposome** suspension. This suspension was centrifuged at 10.degree. to give **liposomes** (10 mL) contg. 1000 units **factor VIII** and 50,000 units aprotinin. These **liposomes** were encapsulated.

IT **9001-27-8**
RL: PROC (Process)
(**liposome** encapsulation of, for oral administration)

L29 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:36363 HCAPLUS
DOCUMENT NUMBER: 94:36363
TITLE: **Pharmaceutical** preparation of the **antihemophilia** factor (**factor VIII**)
PATENT ASSIGNEE(S): Hemker, Hendrik Coenraad, Neth.
SOURCE: Neth. Appl., 9 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

NL 7900459	A	19800722	NL 1979-459	19790119
BE 881238	A2	19800718	BE 1980-199034	19800118
WO 8001456	A1	19800724	WO 1980-NL2	19800118
W: DE, GB, SE, US				
GB 2050833	A	19810114	GB 1980-28797	19800118
GB 2050833	B2	19830330		
DE 3028506	T	19810212	DE 1980-3028506	19800118
SE 8006550	A	19800918	SE 1980-6550	19800918

PRIORITY APPLN. INFO.: NL 1979-459 19790119
WO 1980-NL2 19800118

AB Phospholipid **liposomes** contg. blood-coagulation **factor VIII** [**9001-27-8**] are useful for oral treatment of **hemophilia** A and von Willebrand's disease. Inclusion in the **liposomes** of a charged **lipid**, e.g. a fatty alc. phosphate, phosphatidic acid, or long-chain fatty acid increases the spacing between **liposome** layers and promotes the uptake of **factor VIII** into the **liposomes**. Although only .apprx.30% of the **factor VIII** dose is absorbed into the blood, it is released gradually by the **liposomes**, so that its duration of effectiveness is at least equal to that after i.v. administration. Thus, 50 mL egg **lecithin** soln. (1 g in 10 mL EtOH) was mixed with 10 mL phosphatidic acid soln. (20 mg/mL CHCl3) and the solvents were evapd., leaving a thin **lipid** film on the inner wall of the flask. The **lipids** were dispersed in an isotonic soln. of **factor VIII** conc. (230 units/mL) and the **liposomes** were collected by flotation at 27,000 g. Oral administration of 800 units of **factor VIII** in this form to **hemophilia** patients increased the plasma **factor VIII** level to 10% of the normal value within a short time, and the level remained at .gtoreq.5% of the normal value for 50 h.

IT **9001-27-8**
RL: BIOL (Biological study)
(phospholipid **liposomes** contg., for **hemophilia** treatment)

L29 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:43790 HCAPLUS
DOCUMENT NUMBER: 90:43790
TITLE: Simplified method for preparing pure **antihemophilic** factor concentrate with high yield
PATENT ASSIGNEE(S): Shanbrom, Edward, Inc., USA
SOURCE: Fr. Demande, 13 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2363577	A1	19780331	FR 1976-26640	19760903
FR 2363577	B1	19800509		

AB A procedure is given for concg. and purifying blood-coagulation **factor VIII** (**antihemophilic** factor A) [**9001-27-8**]. The cryoppt. obtained from .apprx.100 L plasma is extd. with water at 25-30.degree. and pH .apprx.7. **Lipids**, denatured proteins, and the prothrombin complex are removed from the ext. by adsorption. Fibrinogen and its denaturation and degrdn. products are pptd. by lowering the temp. to 0-2.degree. after addn. of 3-6% of a polyol. The supernatant, contg. .apprx.80% of the **factor VIII** present in the starting material, is freeze-dried to obtain an **antihemophilic** factor which can be preserved for a long period of time and reconstituted by dissoln. in distd. water or physiol. saline.

IT **9001-27-8P**
RL: PREP (Preparation)
(sepn. and purifn. of)

L29 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:11894 HCAPLUS
DOCUMENT NUMBER: 88:11894
TITLE: Simplified method for preparing a concentrate of **antihemophilic factor VIII** of high purity with high yield
INVENTOR(S): Shanbrom, Edward
PATENT ASSIGNEE(S): Shanbrom, Edward, Inc., USA
SOURCE: Belg., 14 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 845234	A1	19761216	BE 1976-169848	19760816
US 4188318	A	19800212	US 1978-899235	19780424

PRIORITY APPLN. INFO.: US 1975-586948 19750616

AB Blood-coagulation **factor VIII** [**9001-27-8**] is concd. and purified from .gtoreq.100 L of plasma. The cryoppt. is extd. with 2-3 times its vol. in pyrogen-free water. **Lipids**, denatured proteins, and prothrombin complex are removed by adsorption from the ext. Fibrinogen, denatured and degraded products are pptd. with a weak ionic soln. at 1-2.degree.. The supernatant, contg. .gtoreq.80% of the original **factor VIII** present, is sepd., stabilized, clarified, sterilized, and lyophilized.

IT **9001-27-8P**
RL: PREP (Preparation)
(prepn. of highly purified)

L29 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:506725 HCAPLUS
DOCUMENT NUMBER: 87:106725
TITLE: **Antihemophilic** agent
INVENTOR(S): Schwinn, Horst; Heimburger, Norbert
PATENT ASSIGNEE(S): Behringwerke A.-G., Ger.

SOURCE: Ger. Offen., 17 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2550011	A1	19770512	DE 1975-2550011	19751107
DE 2550011	C2	19821125		
NL 7612139	A	19770510	NL 1976-12139	19761102
ES 452923	A1	19771116	ES 1976-452923	19761102
FI 7603165	A	19770508	FI 1976-3165	19761104
IL 50847	A1	19800131	IL 1976-50847	19761104
AT 7608194	A	19800215	AT 1976-8194	19761104
AT 358737	B	19800925		
CH 630805	A	19820715	CH 1976-13920	19761104
DK 7605021	A	19770508	DK 1976-5021	19761105
SE 7612396	A	19770508	SE 1976-12396	19761105
NO 7603776	A	19770510	NO 1976-3776	19761105
ZA 7606647	A	19771026	ZA 1976-6647	19761105
US 4067964	A	19780110	US 1976-739278	19761105
AU 7619341	A1	19780511	AU 1976-19341	19761105
AU 500621	B2	19790524		
CA 1077393	A1	19800513	CA 1976-265060	19761105
JP 52057310	A2	19770511	JP 1976-132782	19761106
JP 60029362	B4	19850710		
BE 848111	A1	19770509	BE 1976-172170	19761108
FR 2330408	A1	19770603	FR 1976-33603	19761108
FR 2330408	B1	19800314		
GB 1563009	A	19800319	GB 1976-46384	19761108

PRIORITY APPLN. INFO.: DE 1975-2550011 19751107

AB **Antihemophilic** compns. contg. blood-coagulation **factor VIII** [**9001-27-8**] are prepd. by extg. ground, blood-free washed placenta with a weakly acidic or weakly basic aq. hypotonic medium, increasing the sp. d. of the ext. by addn. of an inert, H2O-sol. compd., and retrieving the material floating on top of the soln. The material was purified by repetition of the flotation process, by extn. of a dil. aq. soln. of the material with a solvent for **lipids**, by treatment with an aq. alkali soln., by chromatog. or by centrifugation. For example, blood-free, lypophilized placenta tissue was homogenized with 0.05M Na citrate at room temp., the homogenate was centrifuged, and the sediment was discarded. KBr was added to the supernatant to 20% satn., and the mixt. was centrifuged. The floating material was sepd. and treated again by the same flotation procedure with higher-speed centrifugation. The product was suitable for i.v. injection, and contained 200 units blood-coagulation **factor VIII** activity/mL.

IT **9001-27-8**
RL: PROC (Process)
(of placenta exts., isolation of, for **hemophilia** treatment)